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TCT-149

Intracoronary injection of bone marrow derived mononuclear cells, early or late after acute myocardial infarction: Long-term effects on global left ventricular function - Twelve months MRI and long-term clinical results of the SWISS-AMI trial

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Background: Intracoronary administration of autologous bone marrow derived mononuclear cells (BM-MNC) may improve remodeling of the left ventricle (LV) after acute myocardial infarction (AMI) as shown by some, but not all clinical trials published so far. Long-term durability of the treatment effect is less well established.
Methods: In a multi-center study, we randomized 200 patients with large, successfully reperfused ST segment elevation myocardial infarction (STEMI) in a 1:1:1 pattern into an open-labeled control and two BM-MNC treatment groups. In the BM-MNC groups cells were either administered "early", i.e. 5-7 days, or "late", i.e. 3-4 weeks after AMI. Cardiac magnetic resonance imaging (CMR) was performed at baseline (bl) , after 4 and 12 months. The current analysis investigates the change from bl to 12 months in global LV ejection fraction (LVEF), LV-volumes as well as scar size and compares the two treatment groups with control. Furthermore the event rate of a combined clinical endpoint consisting of death, recurrent AMI, recurrent coronary revascularization or rehospitalization for heart failure is computed.
Results: The absolute change in LVEF from bl to 12 months was -1.87±9.84 % for control (mean±SD), -0.88±10.50 % for the early treatment group and -0.70±10.11 % for the late treatment group. The difference between the groups is not significant (p = 0.1571). Changes of NT-proBNP over time are more favorable for BM-MNC groups compared to control. The combined endpoint occurred equally in all three groups (9 vs. 9 vs. 8 events; ns). Overall, 1-year mortality was rather low (2.5%) without significant difference between groups.

Table: Interaction between factor *time* and factor *treatment*

	Time			P for interaction
	baseline	*4 months*	*12 months*	
LVEDV – ml *mean (SD)*				
control	153 (38)	180 (52)	170 (56)	0.1217
early	156 (41)	183 (55)	179 (61)	
late	157 (37)	167 (45)	164 (47)	
LVESV – ml *mean (SD)*				
control	94 (33)	112 (46)	110 (53)	0.3200
early	100 (36)	117 (51)	118 (56)	
late	100 (29)	107 (40)	107 (44)	
nt-proBNP – pg/ml *mean (SD)*				
control	1639 (1304)	686 (822)	643 (1075)	0.0458
early	2082 (2060)	639 (524)	421 (414)	
late	2632 (5218)	749 (698)	429 (405)	

Conclusions: Among patients with STEMI and LV dysfunction following successful reperfusion, intracoronary infusion of BM-MNC either at 5-7 days or 3-4 weeks after AMI, did not improve LV-function at 12 months follow-up, compared to an open labeled, randomized control group.

TCT-150

First-in-man Experience with Transendocardial Injections of Bone Marrow-Derived Mesenchymal Stem Cells in Idiopathic Dilated Cardiomyopathy. The MYOCYTE trial

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Background: In patients (p) with ventricular dysfunction, stem cell therapy has been studied mainly in the subset of ischemic heart disease. Here we present the rationale and the first results of the first-in-man stem cell therapy trial in idiopathic dilated cardiomyopathy (IDC).
Methods: The MYOCYTE trial (NCT 01957826) is a randomized, double blind and placebo-controlled trial that will enroll 70 p with IDC, left ventricular ejection fraction (LVEF) < 45%, II-III NYHA functional class and MVO2 12-21 ml/Kg/min. In a first pilot phase, 10 p will be all treated with bone marrow-derived mesenchymal stem cells (MSC) through 15 transendocardial injections (NOGA XP) in the anterior wall of the left ventricle. In a second phase, 60 p will be radomized in a 3:1 ratio to receive MSC or placebo. MSC are obtained after BM harvesting and 3-4 weeks of culture in GMP facilities (dose: 30-40 million MSC). Primary endpoints include MACE, adverse events, NYHA functional class, Holter monitoring, laboratory parameters and incidence of complications with the use of NOGA XP catheters. Secondary endopints include MVO2 and functional capacity, quality of life questionnaires, perfusion defects by MRI/SPECT, LVEF, ventricular volumes and wall motion score index by echo/MRI, and electromechanical mapping parameters by NOGA XP. Follow-up is scheduled for two years and independent core-labs are included.
Results: So far, six p have been included in the trial, mean age was 60.0±9.6 years and 5 p were male (83%). 83% had hypertension, 50% had diabetes mellitus, 67% dyslipidemia and 33% were smokers. Baseline LVEF was 32.8±8.0% by echocardiography and 38.2±7.7% by MRI. Baseline MVO2 was 17.3±4.7 mL/kg/min, and all p were in II NYHA funcional class. No MACE, adverse and arrhythmic events or procedure-related complications have been observed so far. We have observed 1 sudden death 8.5 months after treatment and 1 contrast-induced renal failure. Echocardiographic follow-up at 3 months is available for 4 p, showing a LVEF of 44.2±5.8%.
Conclusions: To the best of our knowledge this is the first randomized trial with transendocardial injection of MSC in these scenario. MSC injections seem to be safe, and could be potentially beneficial.

TCT-151

Transcatheter Transplantation And In Vivo Tracking Of Human Stem Cell Based Three Dimensional Microtissues In A Porcine Model Of Myocardial Infarction

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Background: The overall low retention-rate of applied single cell suspensions limits the efficacy of current stem cell therapy concepts. Taking advantage of three dimensional (3D) cellular self-assembly prior to transplantation may be beneficial. We investigate the principal feasibility of intramyocardial transplantation of in-vitro generated stem-cell based 3D-microtissues (3D-MTs) in a porcine myocardial infarction model.
Methods: 3D-MTs were generated from iron-oxide (MPIO) labeled human mesenchymal stem cells (hMSCs) using a modified hanging-drop method. Adult pigs (30-40kg) with chronic MI underwent intramyocardial transplantation of 16x103 3D-MTs (1250cells/MT; accounting for 2x107 single hMSCs) into the MI border-zone using a 3D NOGA mapping-guided, transcatheter approach. Follow-up (FU) was performed for up to 6 weeks and in-vivo cell-tracking was done using serial Magnetic Resonance Imaging (MRI), followed by PCR and immunohistochemistry.
Results: Intramyocardial transplantation of hMSC based 3D-MTs was successful in all animals. During FU, no arrhythmogenic or neurological events occurred. Serial MRI displayed intramyocardial presence of the 3D-MTs by detection MPIOs during FU. Intramyocardial retention of 3D-MTs was confirmed by PCR-analysis and was further verified on histology and immunohistochemistry. 3D-MTs were viable, integrated and showed intact micro-architecture.
Conclusions: We demonstrate the feasibility and safety of intramyocardial transplantation of in-vitro generated human stem-cell based 3D-MTs. Multimodal cell-tracking strategies comprising imaging and in-vitro tools allow for in-vivo monitoring and post-mortem analysis of 3D-MTs. 3D cellular self-assembly prior to transplantation may represent a promising application-format for stem-cell based therapies.